

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method for generating antigen-binding fragments of an antibody, comprising:

providing an antibody-producing cell line that is growing in a cell media under conditions to express antibodies;

adjusting the conditions of the cell media to activate at least one endogenous enzyme in said cell media that cleaves said antibodies, wherein the adjusted conditions are selected from the group consisting of temperature conditions and pH conditions; and

incubating said cell line under said conditions so that said antibodies are cleaved into antigen-binding antibody fragments.

2. (Original) The method of Claim 1, wherein said antibodies are cleaved into $F(ab')_2$ fragments.

3. (Original) The method of Claim 1, wherein adjusting the conditions of the cell media comprises adjusting the temperature of the cell media.

4. (Original) The method of Claim 1, wherein adjusting the conditions of the cell media comprises adjusting the pH of the cell media.

5. (Original) The method of Claim 4, wherein adjusting the pH comprises adjusting the pH to about pH 3.5.

6. (Original) The method of Claim 1, further comprising inactivating said at least one endogenous enzyme after incubating said cell line.

7. (Previously presented) The method of Claim 1, further comprising substantially purifying said antigen-binding antibody fragments by affinity chromatography.

8. (Original) The method of Claim 1, wherein said at least one enzyme comprises a serine protease.

9. (Original) The method of Claim 1, wherein said at least one enzyme comprises a cysteine protease.

10. (Original) The method of Claim 1, wherein said at least one enzyme comprises an aspartyl protease.

11. (Original) The method of Claim 1 wherein the cell line comprises cells selected from the group consisting of: Chinese hamster ovary cells, HeLa cells, baby hamster kidney cells, monkey kidney cells, and human hepatocellular carcinoma cells.

12. (Canceled)

13. (Original) The method of Claim 1 wherein the cell media is a protein free media.

14. (Original) The method of Claim 1 wherein the cell media comprises a peptone source.

15. (Original) The method of Claim 1 wherein the cell media is a CD-CHO media.

16. (Original) The method of Claim 1 further comprising inactivating said at least one enzyme by adjusting pH.

17. (Original) The method of Claim 16 wherein inactivating said at least one enzyme comprises inactivating a cysteinyl enzyme.

18. (Original) The method of Claim 17 further comprising activating an aspartyl enzyme by adjusting the pH of the cell media after endogenous cysteinyl enzyme activity has been reduced.

19. (Original) A method for producing $F(ab')_2$ fragments of an antibody, comprising:

providing a cell media comprising a cell line that is growing under conditions to produce a recombinant antibody;

inactivating endogenous cysteinyl enzyme activity in said cell media; and

activating endogenous aspartyl enzyme activity in said cell media, wherein said activation results in cleavage of said recombinant antibody into $F(ab')_2$ fragments.

20. (Original) The method of Claim 19 wherein the cell media is a CD-CHO media.

21. (Original) The method of Claim 19, wherein inactivating endogenous cysteinyl enzyme activity comprises adjusting the pH of the cell media.

22. (Original) The method of Claim 19, wherein inactivating endogenous cysteinyl enzyme activity comprises adding a cysteinyl enzyme inhibitor to the cell media.

Appl. No. : **10/688,198**
Filed : **October 17, 2003**

23. (Original) The method of Claim 22, wherein cysteinyl enzyme inhibitor is E64.

24. (Original) The method of Claim 19, wherein activating endogenous aspartyl enzyme activity comprises adjusting the pH of the cell media.

25. (Original) The method of Claim 19, further comprising purifying said F(ab')₂ fragments from said cell media.

26 - 29 (Canceled)